



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0315]

International Conference on Harmonisation; Draft Guidance for Industry on E2C(R2) Periodic Benefit-Risk Evaluation Report; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “E2C(R2) Periodic Benefit-Risk Evaluation Report.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guidance updates and combines two ICH guidances, “E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs” (E2C guidance) and “Addendum to E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs” (addendum to the E2C guidance). The draft guidance describes the format, content, and timing of a periodic benefit-risk evaluation report (PBRER) for an approved drug or biologic. The harmonized PBRER is intended to promote a consistent approach to periodic postmarket safety reporting among the ICH regions and to enhance efficiency by reducing the number of reports generated for submission to the regulatory authorities.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft

guidance by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE
FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993–0002, or the Office of Communication, Outreach and Development (HFM–40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist the office in processing your requests. The draft guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 301–827–1800. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Regarding the draft guidance:

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Stephen Ripley,
Center for Biologics Evaluation and Research (HFM-17),
Food and Drug Administration,
1401 Rockville Pike, suite 200N,
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301-827-6210.

Regarding the ICH:

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SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory Agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA; and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada, and the European Free Trade Area.

In the Federal Register of May 19, 1997 (62 FR 27470), FDA published a notice announcing the availability of the E2C guidance. In the Federal Register of February 5, 2004 (69 FR 5551), FDA also published the addendum to the E2C guidance to provide needed clarification and additional guidance. Since that time, the pharmacovigilance environment has evolved, prompting reassessment of the role of the periodic safety update report in the spectrum of safety documents submitted to regulatory authorities. This reassessment highlighted several factors that led to consensus for revising the E2C guidance and the addendum to the E2C guidance to enhance their usefulness in light of advances in the field. There has been significant progress in the technology and science of pharmacovigilance, including electronic submission of

individual case safety reports to regulatory authorities, automated data mining techniques, more attention to benefit-risk evaluation, greater emphasis on proactive and documented risk management planning, and increasing recognition that meaningful evaluation of important new risk information should be undertaken in the context of a medicinal product's benefits.

In January 2012, the ICH Steering Committee agreed that a draft guidance entitled "E2C(R2) Periodic Benefit-Risk Evaluation Report" should be made available for public comment. The draft guidance is the product of the E2C(R2) Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the E2C(R2) Expert Working Group.

The draft guidance describes the format, content, and timing of a PBRER for an approved drug or biologic. The PBRER will serve as a common standard for periodic reporting on approved drugs or biologics among the ICH regions. Once this guidance is finalized, applicants can submit a waiver request for submission of the PBRER in the United States in place of a periodic adverse drug experience report for a new drug application, for an abbreviated new drug application, or for a biologics license application. The harmonized PBRER is intended to promote a consistent approach to periodic postmarket safety reporting among the ICH regions and to enhance efficiency by reducing the number of reports generated for submission to the regulatory authorities.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. The Paperwork Reduction Act of 1995

This draft guidance includes information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3520). In accordance with the PRA, before publication of the final guidance document, FDA intends to solicit public comment and obtain OMB approval for any information collections recommended in this guidance that are new or that would represent material modifications to previously approved collections of information found in FDA regulations.

IV. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.regulations.gov>,
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,
or
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Dated: April 6, 2012

David Dorsey,

Acting Associate Commissioner for Policy and Planning.

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